HFA 305

Stamp Date: SEP 21 1998

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION:

ANADA Number: **200-259**

ANADA/Generic Sponsor:
Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

Established Name: Chlortetracycline
Salinomycin sodium
Roxarsone

Trade/Proprietary Name: ChlorMax™
Sacox®
3-Nitro®

Dosage Form: Type A Medicated Articles

Note: This ANADA provides for the combined use of three approved Type A Medicated Articles (ChlorMax chlortetracycline, Sacox salinomycin sodium, and 3-Nitro roxarsone) in Type C Medicated Feeds, rather than a premix incorporating all three of these compounds.

How Supplied: Chlortetracycline: 5, 10 or 50-lb bags
Salinomycin sodium: 50-lb bags
Roxarsone: 50-lb bags

How Dispensed: OTC

Label Claim of Amount of Active Ingredient(s): Chlortetracycline- 50, 65, and 70 g/lb in Type A Medicated Articles
Salinomycin- 30 and 60 g/lb in Type A Medicated Articles
Roxarsone- 10, 20, and 50% (45.4, 90.8, 227 g/lb) in Type A Medicated Articles

Route of Administration: These drugs are administered orally by adding the Type A Medicated Articles to complete broiler feed (Type C Medicated Feed)

Recommended Dosage: Chlortetracycline, 500 grams per ton (.055%)
Salinomycin, 40 to 60 grams per ton (.0044-.0066%)
Roxarsone, 45.4 grams per ton (.005%)

Species:	Broiler Chickens
Indications for use:	For the prevention of coccidiosis in broiler chickens caused by *Eimeria tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti*, and *E. mivati*, including some field strains of *E. tenella* that are more susceptible to roxarsone combined with salinomycin than salinomycin alone, and as an aid in the reduction of mortality due to *E. coli* infections susceptible to such treatments.
Equivalent Product:	ChlorMax Chlortetracycline NADA 46-699 Alpharma Inc.
Pioneer Product/ Listed Product:	Aureomycin Chlortetracycline NADA 48-761 Roche Vitamins, Inc. Sacox Salinomycin sodium NADA 200-075 Roche Vitamins, Inc. 3-Nitro Roxarsone (3-nitro-4-hydroxyphenylarsonic acid) NADA 7-891 Alpharma Inc. Aureomycin®-Sacox®-3-Nitro® Chlortetracycline/Salinomycin/Roxarsone NADA 200-091 Roche Vitamins, Inc.

II. EFFECTIVENESS AND TARGET ANIMAL SAFETY:

ChlorMax and Aureomycin were both found to comply with the results of NAS/NRC and DESI evaluation for effectiveness as published in the Federal Register (61 FR 35949-35958; July 9, 1996). These products approved under the DESI process were found to be equivalent at the codified level 21 CFR § 558.128(d)(1)(viii) of 500 g/ton for chickens (61 FR 35949-35958; July 9, 1996).

The Center's fourth policy letter dated November 2, 1989, as published in the Federal Register on January 30, 1990 (55 FR 3107), states that the approval of a new generic Type A Medicated Article entitles the sponsor to approval of all the feed combinations

for which the pioneer is approved. Bioequivalence and tissue residue studies are not required for approval of the feed use combinations.

Chlortetracycline (ChlorMax-Alpharma) is codified under 21 CFR § 558.128(a)(3). Chlortetracycline (Aureomycin-Roche) is codified under 21 CFR § 558.128(a)(1). Salinomycin sodium is codified under 21 CFR § 558.550. Roxarsone is codified under 21 CFR 558.530. The combination is codified under 21 CFR § 558.550(a)(2) and (d)(1)(xv).

III. HUMAN SAFETY:

a. Tolerances and Safe Concentration of Residues

The tolerances established for the pioneer product apply to the generic product.

Tolerances for the sum of residues of the tetracycline, including chlortetracycline in tissues of chickens, are as follows: (a) 2 parts per million (ppm) in muscle; (b) 6 ppm in liver; (c) 12 ppm in fat (21 CFR § 556.150).

Under NADA 128-686 a tolerance for salinomycin was not required because residue levels in all three broiler tissues (muscle, liver, and skin/fat) were significantly below the established safe concentration.

Tolerances of arsenic (from roxarsone) are established at 0.5 ppm in uncooked muscle tissue and 2 ppm in uncooked edible by-products of broiler chickens with liver as the target tissue (21 CFR § 556.60).

b. Withdrawal Time

Based on the information in 21 CFR § 558.550(d)(1)(xv), a five-day withdrawal time is required for the combination of chlortetracycline, salinomycin and roxarsone.

c. Regulatory Methods for Residues

The regulatory analytical method for the determination of residue of chlortetracycline is a microbiological test using *Bacillus cereus* var. *mycoides* (ATCC 11778). The method is found in Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports and Protocols, Revised October 1968, Reprinted December 1974, National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204.

Under NADA 128-686 a regulatory method for salinomycin was not required because residue levels in all three broiler tissues (muscle, liver and skin/fat) were significantly below the established safe concentration for total residues.

The analytical method for the determination of roxarsone in tissues is a spectrophotometric method. The method, entitled "Arsenic (Total) Residues in Animal

Tissues, Spectrophotometric Method," is published in the Official Methods of Analysis of AOAC International, 16th edition.

IV. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug and Cosmetic Act satisfies the requirements of section 512 (n) of the act and demonstrates that the combination of chlortetracycline, roxarsone and salinomycin, when used under its proposed conditions of use, is safe and effective for its labeled indications.

Attached labeling: Type C Medicated Feed (Blue Bird) - Generic

Lot No._____

NET WEIGHT ON BAG OR BULK

BLUE BIRD SALINOMYCIN/CTC/ROXARSONE
TYPE C BROILER FEED
MEDICATED

For prevention of coccidiosis caused *by Eimeria tenella, E. necatrix, E acervulina, E. maxima, E. brunetti,* and *E. mivati*, including some field strains of *E. tenella* which are more susceptible to roxarsone combined with salinomycin than to salinomycin alone, and as an aid in the reduction of mortality due to *E. coli* infections susceptible to such treatment in broiler chickens.

ACTIVE DRUG INGREDIENTS

Salinomycin sodium.....40 to 60 g/ton
Roxarsone..... 45.4g/t
Chlortetracycline calcium complex equivalent to chlortetracycline HCl .....500 g/ton

GUARANTEED ANALYSIS

Crude Protein, not less than ....._____%
Crude Fat, not less than ....._____%
Crude Fiber, not more than ....._____%

INGREDIENTS

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions listed in Title 21 CFR 501.110.

DIRECTIONS FOR USE

For broiler chickens only; not to be fed for more than five days; not approved for use with pellet binders.

WARNING: Withdraw 5 days before slaughter. Do not feed to laying chickens. May be fatal if accidentally fed to adult turkeys or to horses. When handling or mixing SACOX® premixes, use protective clothing, impervious gloves, eye protection, and an approved dust respirator. Operators should wash thoroughly with soap and water after handling medicated feeds and premixes.

BLUE BIRD FEED MILL
Any Town, USA 12345

4/98